

### Listing of Claims

This listing of claims will replace all prior versions and listings of claims in the application:

#### In the claims

Claims 1-48 (canceled)

49. (currently amended) A method of determining the presence of a target analyte in a sample comprising:

- a) acquiring a first data image of a random array composition comprising:
  - i) a substrate with a surface comprising discrete sites;
  - ii) a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent, ~~wherein at least one of said subpopulations does not contain an optical signature;~~ and
  - iii) a fiducial, wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres;
- b) ~~using said fiducial to register~~ storing said first data image in a computer readable memory, thereby creating to create a registered a stored first data image;
- c) contacting said random array composition with said sample;
- d) acquiring a second data image from said array with said sample;
- e) ~~using said fiducial to register~~ storing said second data image in a computer readable memory, thereby creating to create a registered a stored second data image; and
- f) comparing said first and said second registered stored data images to determine the presence or absence of said target analyte[.], wherein a computer processor registers said first and second stored data images by aligning said fiducial in said first and second stored data images to allow the comparison of said images.

50. (currently amended) The method according to claim 49 wherein said random array comprises a fiber optic bundle and the registration of said first and second stored data images utilize[[s]] a fiducial fiber.

51. (currently amended) The method according to claim 49 wherein said random array comprises microspheres and the registration of said first and second stored data images utilize[[s]] a fiducial microsphere.

52. (currently amended) The method according to claim 49 wherein the registration of said first and second stored data images utilize[[s]] a fiducial template.

53. (previously presented) The method according to claim 49 wherein said bioactive agents are proteins.

54. (previously presented) The method according to claim 49 wherein said bioactive agents are nucleic acids.

Claims 55-60. (canceled)

61. (currently amended) A method of determining the presence of a target analyte in a sample comprising:

- a) providing a registered first data image of a random array composition comprising:
  - i) a substrate with a surface comprising discrete sites;

- ii) a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent, ~~wherein at least one of said subpopulations does not contain an optical signature~~; and
- iii) a fiducial, wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres, wherein said registered first data image is stored in a computer readable memory thereby creating a first stored data image;
- b) contacting said random array composition with said sample;
- c) acquiring a second data image from said array with said sample;
- d) using said fiducial to register storing said second data image in a computer readable memory, thereby creating to create a registered a stored second data image;
- e) comparing said first and said second registered stored data images to determine the presence or absence of said target analyte[.], wherein a computer processor registers said first and second stored data images by aligning said fiducial in said first and second stored data images to allow the comparison of said images.

62. **(previously presented)** The method according to claim 49, wherein said substrate is selected from the group consisting of glass and plastic.

63. **(currently amended)** The method according to claim 49 [[or 62]], 62 or 76, wherein said registration of said first and second data images utilizes a fiducial edge.

64. **(currently amended)** The method according to claim 49 [[or 62]], 62 or 76, wherein at least a first edge of said array is a fiducial edge.

65. **(previously presented)** The method according to claim 51, 52, 53 or 54, wherein said substrate is selected from the group consisting of glass and plastic.

66. **(currently amended)** The method according to claim 49 [[or 62]], 62 or 76, wherein each subpopulation comprises a unique optical signature.

67. **(previously presented)** The method according to claim 66, wherein said unique optical signature is a bleed-through signature.

68. **(currently amended)** The method according to claim 49 [[or 62]], 62 or 76, wherein each subpopulation comprises an identifier binding ligand that will bind a decoder binding ligand whereby the identification of the bioactive agent is elucidated.

69. **(previously presented)** The method according to claim 50, wherein said array comprises at least three fiducials, and each of said fiducials is a fiducial fiber.

70. **(previously presented)** The method according to claim 69, wherein at least one of said fiducial fibers has a different shape from the others.

71. **(previously presented)** The method according to claim 69, wherein at least one of said fiducial fibers has a different color from the others.

72. **(currently amended)** The method according to claim 51 or 61, wherein said registration utilizes at least three fiducials and each of said fiducials is a fiducial microsphere.

73. **(previously presented)** The method according to claim 72, wherein at least one of said fiducial microspheres has a different size from the others.

Application Serial No.: 09/636,387

Filing Date: August 9, 2000

74. **(previously presented)** The method according to claim 72, wherein at least one of said fiducial microspheres has a different color from the others.

75. **(previously presented)** The method according to claim 72, wherein at least one of said fiducial microspheres does not comprise a label.

76. **(new)** The method according to claim 61, wherein said substrate is selected from the group consisting of glass and plastic.